

61. (Amended) The method of claim 59, wherein said small molecule modulator is an agonist of muscle cell growth.

REMARKS

I. Status of the Claims

Claims 1-101 were filed with the application. Claims 1-58 and 63-101 have been withdrawn from consideration. Thus, claims 59-62 are under consideration and have been examined. A copy of these claims is provided in Appendix A.

The disclosure is objected to for informalities. The claims are rejected under 35 U.S.C. §112, second paragraph, under 35 U.S.C. §112, first paragraph (written description and enablement) and under 35 U.S.C. §102. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Objections to Informalities

The examiner has identified a number of informalities, almost all of which are based upon the alleged need for providing full names prior to the first use of acronyms. Applicants traverse on the grounds that the specification may use whatever language best describes the subject matter at hand. Here, the acronyms in question are art accepted and, as such, adding full names to the text adds nothing with respect to the clarity of the specification.

The reference to MCIP2 at page 28, line 2, is correct. The following issues have been addressed by amendments to the specification:

- page 28, line 3, change "SEQ ID:5" to "SEQ ID NO:5"

- references to SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:9 and SEQ ID NO:16 , a supplemental amendment will be filed shortly.
- page 29, line 19, change “7.9” to “7, 9”
- page 30, line 8, change “16also” to “16 also”
- page 83, line 15 delete “(NFAT)”

III. Withdrawal of Claim 70 after Restriction Election

In response to a phone call with the examiner, following applicants’ election of Group XIV, a small molecule agonist was elected for further prosecution. Therefore, claims 63-69 were properly withdrawn. Without explanation examiner also withdrew claim 70, which does not conflict with any of the elections made. Therefore applicants respectfully request that the withdrawal of claim 70 be reversed, and that claim 70 be prosecuted along with the remaining claims, claims 59-62.

IV. Rejections Under 35 U.S.C. §112, Second Paragraph

The examiner has rejected claims 59-62 under §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter. The examiner first objects to use of the word “modulation” as not defining whether the regulation is up or down. This objection is improper. The very essence of the present claims is to identify small peptides that may modify MCIP expression *in either direction – up or down*; hence the use of the word *modulation* is the very point of the claim, and very much correct. Reconsideration and withdrawal of the rejection is respectfully requested.

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The examiner further rejects claim 59 as it is alleged that the claim does not make clear how a peptide is administered to a muscle cell. However, the claim is purposefully generic in this regard, being drawn to a variety of methods for administering a peptide to a cell, many of which are described in the specification (see, e.g., pages 66-72 for a variety of delivery methods; see also Example 2, page 95, lines 13-20; page 96-97 lines 28-31 and 1-10; Example 3, page 99, lines 14-20). Reconsideration and withdrawal of the rejection is respectfully requested.

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The examiner also objects to the limitation "mammal" in claim 60 as having insufficient antecedent basis. There is no need for antecedent basis since the term mammal is properly introduced in claim 60 as "a mammal" and not "said mammal." Reconsideration and withdrawal of the rejection is respectfully requested.

V. Rejections Under 35 U.S.C. §112, First Paragraph (Written Description)

The examiner has rejected claims 59-62 under 35 U.S.C. §112, first paragraph, alleging that the inventors do not have possession of a small molecule agonist of muscle cell growth. The examiner further cites to the *Lilly* case to support his rejection and statement that the disclosure "insufficiently provides a representative number of species to describe the genus that is 'peptide.'" Applicants submit that the examiner is attempting to extend a rule of law from *Lilly* that is uniquely applicable to DNA molecules and is not valid when applied to the case at hand.

Lilly and its subsequent cases have *not* required that, to be adequately described, an invention must *always* be specifically described so completely as in the manner in which *Lilly* required for those *particular* DNA molecules, nor do the cases require that a genus must be described in its entirety. Further, *Lilly* was directed to the very unique problem created by attempting to claim a genus of DNA molecules by describing a single species. The courts

properly recognized that the degeneration of the genetic code and the structural dissimilarity of DNA's between species would not automatically allow one of skill in the art to have possession of a DNA from, for example, most or all mammalian species simply by having possession of a rat sequence.

This logic does not hold true for a claim that refers to small molecules. The agonists claimed in the invention are members of a broad and well-understood genus, the possession of which is possible merely by opening up a catalog and ordering any of a variety of available species. Their method of discovery, isolation, application, and use are explicitly described in the patent, and thus one of skill in the art could conclude, as can be seen in the Bush Declaration (see para. 10 conclusion), that the inventors did indeed have "possession" of the claimed invention – a level of possession that meets the standards required according to the MPEP and the controlling case law.

Recent cases elaborating on the holdings of *Lilly* show that the standard of review varies depending on the invention, and whether it can be described in more than a functional way. See *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013 (Fed. Cir. 2002). It is not proper to automatically apply the *Lilly* standard to any and all cases where there is a genus claimed because, as stated above, *Lilly* deals with a very unique problem presented by DNA's. Both *Lilly* and *Enzo* require that "the disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim." The important point of both cases is that function alone, wishful thinking, cannot support a set of claims to the molecules behind that function. However, it does not set up a proscription against the generic claiming of inventions.

In this regard, it is thus of utmost importance to note the guidance that is found in the MPEP on satisfying the requirements of written description, for example, MPEP §2163 which

states that “the examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed, *Wertheim*, 541 F.2d at 262, 191 USPQ at 96.” As can be seen in the Bush Declaration (see paras. Sections 9 and 10), there is actually strong evidence that counters the examiner’s assertions, namely, that the specification does provide more than adequate support for the claims.

Furthermore, the examiner is directed by the MPEP §2163 II(A)(2) to “review the entire application to understand how applicant provides support for the claimed invention including each element and/or step.” Applicants contend that, upon such review, one would find more than adequate support in this application for the present claims. Pages 15 and 16 describe known methods of modulating MCIP levels with T3 thyroid hormone or oxidative stress. Pages 66-67 describe the use of mimetics or suicide substrates to modulate MCIP1 expression. Pages 68-72 are replete with examples describing delivery methods to a variety of target cells. Finally, and perhaps most pertinently, pages 75-81 describe in great detail how one would screen for and obtain modulators of MCIP that could then be used to practice the invention.

The policy of the §112 written description requirement is not to force the inventors to have a working model in hand at the time of submission. The written description requirement has several policy objectives. “The ‘essential goal’ of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed.” *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977). Another objective “is to put the public in possession of what the applicant claims as the

invention.” *Lilly*, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998). Both of these policy objectives are satisfied by the description in the present application, and the examiner is attempting to go beyond these objectives, arguing in favor of working examples for the entire genus.

However, the inventors need not present an actual working model. Applicants again refer the examiner to MPEP §2163, stating “an applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as *words*, structures, *figures*, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997)” (emphasis added). As Dr. Bush has himself stated in his affidavit, “this specification provides ample guidance for one of skill in the art to screen for, discover, and apply any of a variety of agonists that would both modulate muscle cell growth and/or MCIP1.”

The above statements, Dr. Bush’s Declaration and a proper reading of *Lilly* and *Enzo* as those courts intended, illustrate that the present invention does indeed contain an adequate written description. Therefore, applicants respectfully request that the rejection be withdrawn.

VI. Rejection Under 35 U.S.C. §112, First Paragraph (Enablement)

Claims 59-62 have also been rejected for alleged lack of enablement. The examiner has undertaken an extensive *In re Wands* analysis and, after a lengthy discussion, concludes that this field is unpredictable, that to practice the invention would require undue experimentation as a result of that unpredictability, and that the skilled artisan would not be able to predict success in using the claimed methods. In light of these conclusions, the examiner thus argues that the specification is not enabling. Applicants respectfully traverse this rejection.

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Though the Office Action is extensive, there is no *specific* support for the examiner's conclusions that "the skilled artisan would have not known what and how a peptide agonist is administered to target muscle cells without degradation or cytotoxicity." In direct contrast to these statements, Dr. Bush has applied the suggested methods of the specification, and has discovered "small molecules capable of increasing expression of endogenous MCIP1 protein in the heart." Dr. Bush's discovery of two small molecule agonists of MCIP1 that also modulate muscle cell growth, coupled with his statements, is in direct contrast to the Examiner's position that the specification is not enabling. His data (see Bush Declaration, para. 9, FIGS. A-C thereof) is directly supportive of the specification as it shows that the invention works as claimed.

Applicants draw the Examiner's attention to *In re Marzocchi*, 169 USPQ 370 (CCPA 1971), stating "As a matter of Patent Office practice, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein." Furthermore, *Marzocchi* holds that "a rejection for failure to teach how to make and/or use ... can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling." Finally, in regards to examiner's burden, *Marzocchi* holds "it is incumbent upon the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure."

Applicants assert that, in addition to failing to properly explain why one would doubt the truth or accuracy of the statements contained in the specification, the examiner has also failed to provide evidence or scientific support to refute the statements in the specification. Furthermore, the Bush Declaration provides the "suitable proofs" that show enablement of this claimed invention. As a result of these proofs, and in light of the above statements, applicants assert that the rejected claims do in fact enable one of skill in the art to practice the invention. Therefore, it is respectfully requested that the claims be reconsidered and the rejection be withdrawn.

VII. Rejection Under 35 U.S.C. §102

Claims 59-62 are rejected by the Examiner under 35 U.S.C. §102(b) as allegedly being anticipated by Miyazaki *et al.* (1996). This reference claims the ZAKI-4 protein, also known as MCIP2. The claims have thus been amended to read only on MCIP1. Therefore applicants respectfully request that this rejection be withdrawn.

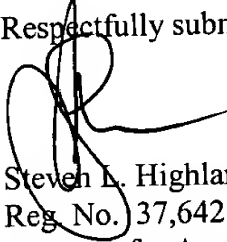
Claims 59-62 are also rejected under 35 U.S.C. §102(a) as being anticipated by Fuentes *et al.* (July 1, 2000). In response, applicants submit the Inventors' Declaration under 37 C.F.R. §1.131 and supporting document. This declaration and the document contained should sufficiently swear behind this reference. As such, applicants respectfully request that this rejection also be withdrawn.

Claims 59-62 are finally rejected under 35 U.S.C. §102(a) as being anticipated by Rothermel *et al.* (2000). In response, applicants submit the Inventor's Declaration under 37 C.F.R. §1.132. This declaration explains that the authors of the paper are the current inventors, and that no other authors listed on the papers contributed an inventive step and thus should not be listed as inventors. As such, applicants respectfully request that this rejection also be withdrawn.

VIII. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to this effect is earnestly solicited. Should Examiner Liu have any questions regarding this response, he is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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APPENDIX A: MARKED UP COPY OF AMENDED CLAIMS

59. (Amended) A method of modulating muscle cell growth comprising:

- (a) providing a small molecule modulator of MCIP₁ expression; and
- (b) administering said modulator to a muscle cell

whereby administration of said modulator results in modulation of muscle cell growth.

61. (Amended) The method of claim 59, wherein said small molecule modulator is an agonist of muscle cell growth.

APPENDIX B: CLEAN COPY OF PENDING CLAIMS (UNOFFICIAL)

59. A method of modulating muscle cell growth comprising:

- (a) providing a small molecule modulator of MCIP₁ expression; and
- (b) administering said modulator to a muscle cell

whereby administration of said modulator results in modulation of muscle cell growth.

60. The method of claim 59, wherein said muscle cell is located in a mammal.

61. The method of claim 59, wherein said small molecule modulator is an agonist of muscle cell growth.

62. The method of claim 61, wherein said agonist is a small molecule.

70. The method of claim 60, further comprising administering to said mammal a pharmaceutical agent used to treat cardiac disease.

APPENDIX C: MARKED UP COPY OF SPECIFICATION

Page 28, paragraph 1:

The present invention also provides, in another embodiment, genes encoding MCIP1 and MCIP2. Genes for human MCIP1 (SEQ ID NO:1), MCIP2 (SEQ ID NO:3) and MCIP3 (SEQ ID:5 and 17[6]) have been identified. Also provided are MCIP1 and MCIP2 from mouse (SEQ ID NOS:7 and 9). The present invention is not limited in scope to these genes, however, as one of ordinary skill in the could, using these nucleic acids, readily identify related homologs in various other species (*e.g.*, rat, rabbit, dog, monkey, gibbon, human, chimp, ape, baboon, cow, pig, horse, sheep, cat and other species).

Page 29, paragraph 2:

As used in this application, the term "a nucleic acid encoding a MCIP" refers to a nucleic acid molecule that has been isolated free of total cellular nucleic acid. In preferred embodiments, the invention concerns a nucleic acid sequence essentially as set forth in SEQ ID NOS: 1, 3, 5, 7, 9 and 16. The term "as set forth in SEQ ID NOS: 1, 3, 5, 7, 9 or 16" means that the nucleic acid sequence substantially corresponds to a portion of SEQ ID NO:1, 3, 5, 7, 9 or 16. The term "functionally equivalent codon" is used herein to refer to codons that encode the same amino acid, such as the six codons for arginine or serine (Table 1, below), and also refers to codons that encode biologically equivalent amino acids, as discussed in the following pages.

Page 30, first paragraph:

Allowing for the degeneracy of the genetic code, sequences that have at least about 50%, usually at least about 60%, more usually about 70%, most usually about 80%, preferably at least about 90% and most preferably about 95% of nucleotides that are identical to the nucleotides of SEQ ID NOS:1, 3, 5, 7, 9 and 16 are contemplated. Sequences that are essentially the same as those set forth in SEQ ID NOS:1, 3, 5, 7, 9 and 16 also may be functionally defined as sequences that are

capable of hybridizing to a nucleic acid segment containing the complement of SEQ ID NOS:1, 3, 5, 7, 9 and 16 under standard conditions.

Page 83, second paragraph:

GST-MCIP1 fusions were expressed from the bacterial expression plasmid pGEX-CS (T.D. Parks, et al. 1994). Luciferase reporter plasmids, Mb-luc and IL-2-luc, were constructed in pGL3 (Promega) by inserting promoter/enhancer regions from genes encoding human myoglobin (Chin *et al.*, 1998) or IL-2 (Clipstone *et al.*, 1992), respectively. In addition, a synthetic enhancer consisting of three copies of a high affinity MEF2 binding sequence from the desmin promoter (Naya *et al.*, 2000) was linked to a minimal promoter (hsp68) and inserted into pGL3 yielding the des-MEF-luc reporter. The β -galactosidase reporter plasmid pCMV-lacZ (J. Grayson, et al. 1998), and expression vectors encoding constitutively active forms of NFAT [(NFAT)] (Molkentin *et al.*, 1998), calcineurin (CnA*) (Chin *et al.*, 1998, O'Keefe *et al.*, 1992), or calmodulin dependent protein kinase type IV (CaMKIV) (Ho *et al.*, 1996), were previously described. The identity of plasmid constructions was confirmed by restriction mapping and partial DNA sequencing.